22. The method of claim 14 wherein said composition is the SP8 antibody or binding fragment thereof.

23. The method of claim 14 wherein said Meningitis Related Homologous Antigenic Sequence is QQQPKA.

24. The method of claim 16 wherein said composition is the SP8 antibody or binding fragment thereof.

25. The method of claim 16 wherein said Meningitis Related Homologous Antigenic Sequence is QQQPKA. --

REMARKS

Applicants submit this Preliminary Amendment to insert proper references to SEQ ID NOS of the Sequence Listing filed concurrently, to indicate the insertion point for the Sequence Listing and to correct two typographical errors in the specification, one at page 1, line 2, and another at page 68, line 27. The amino acid sequence on page 68, line 27, is being amended in order to correct an obvious typographical error. The amendment is supported in Table 1, at line 3, and in Figure 1, at amino acid region 313-319, of the as-filed application. Thus, no new matter is introduced by this amendment. Applicants respectfully request examination on the merits of this application.

Support for the new claims can be found in the instant specification at pages 74-76 and claim 13. Please note that the instant specification discusses

> [a] "clearance" assay designed to measure the level of bacteremia in baby rats challenged with infection by the meningitis-causing organism *H. influenzae*.

Instant Specification at page 74.

Additionally, the instant specification describes

> a significant, detectable clearance of Hib organisms by the SP8 antibody. These data demonstrate that antibody directed against the *S. pneumoniae* MRHAS amino acid sequence QQQPPKA has some protective effect *in vivo* against challenge by another meningitis-causing organism *H. influenzae* type b. Since the amino acid sequence of MRHAS from *H. influenzae* type b differs from the MRHAS in *S. pneumoniae*, the data demonstrate that an antibody directed to an MRHAS, such as SP8, can be used *in vivo* to protect the animal from infection from a diverse array of meningitis-causing organisms. The protective effect may block the common MRHAS-mediated entry of the meningitis-causing organisms into carrier monocytes.

Instant Specification at page 76.

The instant specification provides ample guidance to those of skill in the peptide synthesis art, both synthetic and recombinant, to teach how to make and use the products of claims 14-17.

Further, we point out that several publications provide evidence that the "clearance" assay employed in the instant specification is the art-accepted model for measure the level of infection and clearance of bacteria or virus in baby rats challenged with infection by the meningitis-causing organism. This animal model is a recognized model for determining efficacy of vaccine candidates as well.

Two publications by Saukkone, K., *et al.* (Microb. Path. 3: 261 (1987) and Vaccine 7: 325 (1989)) describe experiments which showed that antibodies against the class 1 Outer Membrane Protein (OMP) were bactericidal and highly protective against bacterial challenge with *N.meningitidis* in the infant rat model. Alternatively, Green *et al.* (Infection and Immunity 59:3191 (1991) used an *in vitro* assay instead of the infant rat model to test the efficacy of the mixture of new antibodies. Green *et al.* showed that polyclonal and

monoclonal antibodies to P4 can be prepared and mixed to produce (synergistic) bactericidal (BC) activity against *H. influenzae*.

Applicants propose to amend FIGURE 2 as show in red on the attached copy. With the Examiner's approval, the changes will be made to the formal drawings in due course. Support for the proposed amendment may be found on page 20, Table 1, in the line that reads:
"MRHASRV-4 Rubella Structural LPQPPCA" of the as-filed specification. Further support for said amendment may be found at page 26, Table 4, in the line that reads:
"Rubella Structural 313-319 LPQPPCA" of the as-filed specification. Applicants respectfully request that entry of the amendment to change the "Arg" to Cys" as residue 319 of Figure 2, is proper. If the Examiner has any concerns, it is requested that she immediately contact the undersigned at the telephone number listed below.

It is believed that no additional fees are required; however, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 19-0741. It is further believed that no petition for an extension of time under 37 C.F.R. § 1.136 is required. However, should such a petition be required, applicant hereby petitions the Commissioner for an extension of time, and authorizes the Commissioner to charge the necessary petition fee to Deposit Account No. 19-0741.

Respectfully submitted,

December 11, 1997
Date

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